PROC (BAYL UNIV MED CENT)
2021;34(5):545–549

https://doi.org/10.1080/08998280.2021.1925810

Taylor & Francis
Taylor & Francis Group

Burden of arrhythmias and associated in-hospital mortality in acute decompensated diabetes mellitus

Upenkumar Patel, MBBS, MPH[a], Rupak Desai, MBBS[b], Rezwan Munshi, MD[a], Palakkumar Patel, MD[a], and Amgad N. Makaryus, MD[c,d]

[a]Department of Internal Medicine, Nassau University Medical Center, East Meadow, New York; [b]Division of Cardiology, Atlanta VA Medical Center, Decatur, Georgia; [c]Department of Cardiology, Nassau University Medical Center, East Meadow, New York; [d]Department of Cardiology, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell Health, Manhasset, New York

ABSTRACT

To gain understanding of the burden of cardiac arrhythmias in patients with acutely decompensated diabetes mellitus (ADDM) on a large scale, we reviewed data on ADDM patients and subtypes of arrhythmias from the National Inpatient Sample from 2010 to 2014. The frequency and prevalence of cardiac arrhythmias were measured, as well as outcomes. Among 874,107 hospitalized ADDM patients identified, 87,970 (10.1%) developed arrhythmias. The ADDM-arrhythmia cohort showed higher all-cause mortality (1.4% vs 0.3%; adjusted odds ratio 2.58, 95% confidence interval 2.39–2.79, $P < 0.001$), prolonged hospital stays (4.2 ± 4.8 vs 3.3 ± 3.4 days), and higher hospital charges ($32,609 vs $23,741) compared to those without arrhythmias ($P < 0.001$). The prevalence of supraventricular arrhythmia (atrial fibrillation, supraventricular tachycardia, and atrial flutter) and ventricular arrhythmia (ventricular tachycardia and ventricular fibrillation) was 2965 and 446 per 100,000 ADDM-related hospitalizations, respectively. The prevalence of any arrhythmias and atrial fibrillation in ADDM patients increased by 20.4% and 38.1%, respectively. The highest increase in the prevalence of arrhythmia among ADDM patients was observed in adults aged 18 to 44 years (22.5%).

KEYWORDS Acute decompensated diabetes mellitus; arrhythmia; mortality; prevalence; trends

Diabetes mellitus (DM) is on the rise worldwide and is one of the leading causes of cardiovascular morbidity and mortality.[1] Although coronary artery disease remains one of the most common diabetic cardiovascular adverse effects, arrhythmias are also frequently reported in DM patients.[2] The multifactorial mechanisms contributing to cardiac arrhythmias in DM include autonomic dysfunction, cardiac remodeling, and inflammation, as well as hemodynamic, metabolic, and electrolyte factors.[3,4] Diabetic ketoacidosis and/or hyperosmolar hyperglycemic syndrome, considered acute decompensation states of DM, are potentially fatal diabetic emergencies in type 1 and type 2 DM.[5] We sought to measure the cumulative frequency and temporal trends in the prevalence of cardiac arrhythmias and outcomes in a nationwide cohort of patients primarily admitted for acutely decompensated DM (ADDM) in the United States.

METHODS

The study cohort was retrieved from the National Inpatient Sample datasets (2010–2014), a part of the Healthcare Cost and Utilization Project, organized and supported by the Agency for Healthcare Research and Quality.[6] The National Inpatient Sample is the largest all-payer publicly accessible health care database in the United States inclusive of inpatient encounters. It comprises records of ~7 million unweighted and ~35 million weighted hospital encounters each year. The data are initially unweighted and later changed to weighted data using an algorithm provided by the Healthcare Cost and Utilization Project, which allowed us to measure national estimates.[6]

Corresponding author: Amgad N. Makaryus, MD, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell and Chairman, Department of Cardiology, Nassau University Medical Center, 2201 Hempstead Turnpike, East Meadow, NY 11554 (e-mail: amakaryu@numc.edu)

The authors report no conflicts of interest.

Received March 7, 2021; Revised April 22, 2021; Accepted April 26, 2021.

Codes from the International Classification of Diseases, Ninth Revision, Clinical Modification were used to identify adult hospitalizations between 2010 and 2014 for ADDM (diabetic ketoacidosis, 250.10–250.13; hyperglycemic hyperosmolar state, 250.20–250.23) and arrhythmias (atrial fibrillation, 427.31; atrial flutter, 427.32; supraventricular tachycardia, 427.0; ventricular fibrillation, 427.41; ventricular tachycardia, 427.1). To keep the dataset uniform, the dataset was analyzed until 2014, as data from 2015 and onwards used ICD-10-CM codes. These validated ICD-9 CM codes have been utilized in previously published studies during this time.[7–9] Discharges related to patients under 18 years and patients without DM were excluded from the study cohort. Unspecified arrhythmias and clinically nonrelevant arrhythmias were not analyzed in this study.

The Pearson chi-square test and Student *t* test were used to evaluate categorical and continuous variables, respectively. The trends in the frequency of arrhythmias in hospitalized ADDM patients were analyzed by the linear-by-linear association test. After adjusting for baseline characteristics and comorbidities, a two-step hierarchical multivariate regression model was utilized to estimate the risk of inpatient mortality secondary to any arrhythmia. IBM SPSS Version 22 (Armonk, NY) was used for all statistical analyses.

RESULTS

A total of 874,107 hospitalizations for ADDM were identified from 2010 to 2014. Of these, 87,970 encounters (10.1%) were associated with arrhythmias (mean age, 46.4 ± 19.6 years; 50.4% women). Among hospitalized patients with ADDM, the prevalence of arrhythmia was highest in those aged 18 to 44 years (48.9%). The cohort with arrhythmia consisted more often of white (59.0%) and Medicare enrollees (32.0%) with weekday (73.0%) and nonelective (97.4%) admissions. The ADDM-arrhythmia cohort was more likely managed at large (56.4%), nonprofit private (74.2%), urban-teaching hospitals (50.6%) in the southern (43.6%) part of the US. The ADDM-arrhythmia cohort had a higher prevalence of major comorbidities than the nonarrhythmia group. The cohort with arrhythmia had worse hospitalization outcomes including higher inpatient mortality (1.4% vs 0.3%, $P < 0.001$), a longer hospital length of stay (4.2 ± 4.8 vs 3.3 ± 3.4 days, $P < 0.001$), and higher hospital charges ($32,609 vs $23741, $P < 0.001$) compared with the cohort without arrhythmia ($P < 0.001$) *(Table 1)*.

As shown in *Figure 1*, the overall frequency of arrhythmia was 10,064 per 100,000 hospitalizations for ADDM; the prevalence of supraventricular arrhythmias (atrial fibrillation, supraventricular tachycardia, and atrial flutter) and ventricular arrhythmias (ventricular fibrillation and ventricular tachycardia) were 2965 and 446 per 100,000 admissions for ADDM, respectively. The prevalence of any arrhythmia in this group of patients increased from 9.3% in 2010 to 11.2% in 2014 (a 20.4% relative increase, $P_{trend} < 0.001$). The prevalence of atrial fibrillation increased from 2.1% in 2010 to 2.9% in 2014 (38.1% relative increase, $P_{trend} < 0.001$) *(Figure 2a)*. Among admissions for ADDM from 2010 to 2014, the prevalence of arrhythmias in male and female patients increased by 19.8% and 22.1%, respectively ($P_{trend} < 0.001$) *(Figure 2b)*. The rising trends in arrhythmia among hospitalized ADDM patients rose by 22.5% in those aged 18 to 44, 19.1% in those aged 45 to 64, and 10.1% in those aged ≥65 during the study period *(Figure 2c)*.

The ADDM cohort with arrhythmia demonstrated nearly 4 times higher odds of all-cause mortality on an unadjusted analysis (odds ratio 4.28, 95% confidence interval 3.99–4.58, $P < 0.001$) and 2.5 times higher odds of all-cause mortality on an adjusted multivariable analysis (odds ratio 2.58, 95% confidence interval 2.39–2.79, $P < 0.001$) as compared to the cohort without arrhythmia.

DISCUSSION

This study revealed a substantial surge (20% relative increase) in the prevalence of cardiac arrhythmias in hospitalized ADDM patients between 2010 and 2014. This increase was most frequently noted in young (18–44 years) and female patients. Moreover, the incidence of arrhythmia during ADDM hospitalizations proved to be a significant predictor of poor outcomes, with an increased odds of all-cause mortality, prolonged hospital stays, and higher hospital charges compared with the cohort without arrhythmia.

Life-threatening cardiac arrhythmias are rarely reported in DM patients with acute decompensation, and those reported are typically found to be reversible with appropriate treatment.[10] Fluid electrolyte imbalances such as hypokalemia, hyperkalemia, hypophosphatemia, hypocalcemia, hypomagnesemia, and acid-base imbalance are known to contribute to cardiac arrhythmias in DM patients.[11–14] The recent emphasis on the requirement of telemetry monitoring for DM patients with an acute decompensated state and resultant frequent successful detection of abnormal heart rhythms in modern clinical practice could be the primary factor for the rising prevalence of arrhythmias noted among ADDM patients in our study.

A Danish nationwide population-based study showed that young people with DM have a higher risk of sudden cardiac death than those without DM. Cardiovascular diseases were the leading cause of death among this group.[15] Similarly, our study showed that arrhythmias were more prevalent in young adults aged 18 to 44 years with DM decompensation. The higher odds of in-hospital mortality in hospitalized patients for ADDM with arrhythmia (2.5-fold higher) as compared to those without arrhythmia is of particular importance. The mortality associated with diabetic ketoacidosis has decreased over the years with improvements in the management of ADDM.[16] However, ADDM is reported to be frequently complicated by septic shock, acute kidney injury, pulmonary edema, respiratory failure, cardiac arrest, and cardiac/extracardiac comorbidities, consistent

Table 1. Baseline characteristics and outcomes of decompensated diabetes mellitus inpatient encounters with versus without arrhythmia

Variable	Decompensated diabetes		
	No arrhythmia	Any arrhythmia	*P value*
Weighted N	786,137	87,970	
Age (years) at admission			
Mean age ± SD	41.46 ± 16.42	46.37 ± 19.64	<0.001
18–44	58.3%	48.9%	
45–64	32.5%	31.1%	
≥65	9.1%	20.0%	
Sex			<0.001
Male	51.4%	49.6%	
Female	48.6%	50.4%	
Race			<0.001
White	55.0%	59.0%	
African American	28.8%	27.2%	
Hispanic	11.8%	9.2%	
Asian or Pacific Islander	1.1%	1.3%	
Native American	0.9%	0.7%	
Other	2.5%	2.6%	
Primary expected payer			<0.001
Medicare	22.8%	32.0%	
Medicaid	26.8%	22.7%	
Type of admission			<0.001
Nonelective	96.9%	97.4%	
Elective	3.1%	2.6%	
Admission day			<0.001
Weekday	73.8%	73.0%	
Weekend	26.2%	27.0%	
Median household income national quartile for patient ZIP code			<0.001
0–25	39.2%	37.6%	
26–50	27.2%	25.8%	
51–75	20.8%	21.8%	
76–100	12.8%	14.8%	
Location/teaching status of hospital			<0.001
Rural	14.7%	13.2%	
Urban nonteaching	38.1%	36.3%	
Urban teaching	47.1%	50.6%	
Region of hospital			<0.001
Northeast	16.6%	16.2%	
Midwest	21.7%	23.0%	
South	42.1%	43.6%	
West	19.5%	17.2%	
Control/ownership of hospital			<0.001
Government, nonfederal	14.8%	12.9%	
Private, nonprofit	70.9%	74.2%	
Private, investor-owned	14.3%	12.9%	
Comorbidities			
Alcohol abuse	6.8%	7.2%	<0.001
Deficiency anemias	14.9%	18.8%	<0.001
RA/collagen vascular diseases	1.2%	1.6%	<0.001
Congestive heart failure	4.0%	10.6%	<0.001
Acute myocardial infarction	1.1%	3.0%	<0.001
Coronary atherosclerosis	9.5%	17.0%	<0.001
Chronic pulmonary disease	11.4%	14.0%	<0.001
Drug abuse	10.4%	9.1%	<0.001
Hypertension	45.2%	53.5%	<0.001
Hypothyroidism	9.9%	11.2%	<0.001
Liver disease	3.6%	3.7%	0.106
Fluid and electrolyte disorders	61.5%	74.3%	<0.001
Obesity	9.2%	11.7%	<0.001
Peripheral vascular disorders	2.7%	4.4%	<0.001
Pulmonary circulation disorders	0.7%	2.2%	<0.001
Renal failure	12.3%	15.3%	<0.001
Valvular disease	1.0%	3.5%	<0.001
Outcomes			
All-cause in-hospital mortality	0.3%	1.4%	<0.001
Total hospital charges (mean)	$23,741	$32,609	<0.001
Length of stay (days) (mean ± SD)	3.27 ± 3.38	4.23 ± 4.83	<0.001
Disposition of patient			<0.001
Routine	82.3%	74.2%	
Transfer to short-term hospital	1.0%	1.6%	
Other transfers (SNF, ICF, other facility)	4.7%	9.3%	
Home health care	6.8%	9.7%	
Against medical advice	4.9%	3.8%	

ICF indicates intermediate care facility; RA, rheumatoid arthritis; SNF, skilled nursing facility.

(*Continued on next page*)

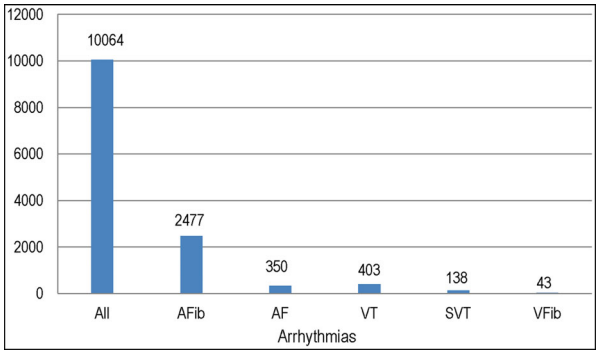

Figure 1. Frequency of all arrhythmias and subtype of arrhythmia per 100,000 hospitalizations for patients with decompensated diabetes mellitus. AFib indicates atrial fibrillation; AF, atrial flutter; VT, ventricular tachycardia; SVT, supraventricular tachycardia; VFib, ventricular fibrillation.

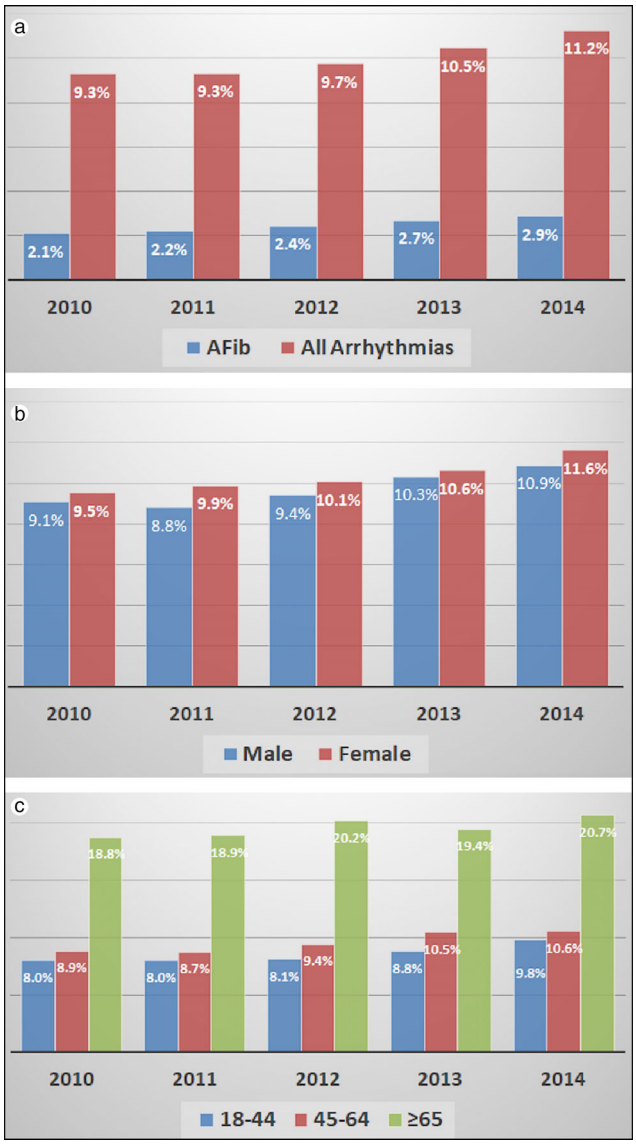

Figure 2. **(a)** Percent distribution of atrial fibrillation (AFib) and all arrhythmias among patients with decompensated diabetes mellitus. **(b)** Percent distribution of all arrhythmias among patients with decompensated diabetes mellitus stratified by sex and **(c)** stratified by age.

with our study. These complications could potentially result in higher mortality among patients with ADDM with arrhythmias. One of the reasons for a prolonged hospital course could be the additional diagnostic workup and management associated with arrhythmias, which ultimately leads to higher utilization of health care resources.

The potential limitations of this study include the administrative nature of the National Inpatient Sample dataset, diagnostic coding errors, inability to trace specific patient encounters longitudinally, the possibility of overcalculation of disease burden due to multiple admissions of the same patient, and an unknown record of medication and insulin administration in DM patients as well as the specific cause of death. As it is known that atrial and ventricular arrhythmias have different prognoses, the impact of any arrhythmia on hospitalization outcomes cannot be assessed directly. It is well established that coronary artery disease, heart failure, and valvular disease are major risk factors for developing cardiac arrhythmias in the general population. Our study showed a higher burden of all these comorbidities among the ADDM cohort with arrhythmia, which could be the confounding factors in hospitalization outcomes.

In conclusion, the prevalence of arrhythmias increased significantly in the US among patients hospitalized for ADDM from 2010 to 2014. The incidence of arrhythmia was linked to poor outcomes and significant health care resource utilization in such patients. This study proposes that early acknowledgment and prompt management of rhythm disturbances among DM patients with acute decompensation may be helpful in decreasing the burden of pertinent in-hospital mortality and financial burden.

ORCID

Rezwan Munshi http://orcid.org/0000-0002-4472-775X
Amgad N. Makaryus http://orcid.org/0000-0003-2104-7230

1. Garcia MJ, McNamara PM, Gordon T, Kannel WB. Morbidity and mortality in diabetics in the Framingham population. Sixteen year follow-up study. *Diabetes*. 1974;23(2):105–111. doi:10.2337/diab.23.2.105.
2. Koektuerk B, Aksoy M, Horlitz M, Bozdag-Turan I, Turan RG. Role of diabetes in heart rhythm disorders. *World J Diabetes*. 2016;7(3):45–49. doi:10.4239/wjd.v7.i3.45.
3. Grisanti LA. Diabetes and arrhythmias: pathophysiology, mechanisms and therapeutic outcomes. *Front Physiol*. 2018;9:1669. doi:10.3389/fphys.2018.01669.
4. Makaryus AN. Ventricular arrhythmias in dialysis patients. *Rev Cardiovasc Med*. 2006;7(1):17–22.
5. Karslioglu French E, Donihi AC, Korytkowski MT. Diabetic ketoacidosis and hyperosmolar hyperglycemic syndrome: review of acute decompensated diabetes in adult patients. *BMJ*. 2019;365:l1114. doi:10.1136/bmj.l1114.
6. Agency for Healthcare Research and Quality. Healthcare Cost and Utilization Project (HCUP). Content last reviewed March 2021. https://www.ahrq.gov/data/hcup/index.html.
7. Desai R, Patel U, Singh S, et al. The burden and impact of arrhythmia in chronic obstructive pulmonary disease: Insights from the

National Inpatient Sample. *Int J Cardiol*. 2019;281:49–55. doi:10.1016/j.ijcard.2019.01.074.
8. Desai R, Patel U, Deshmukh A, Sachdeva R, Kumar G. Burden of arrhythmia in recreational marijuana users. *Int J Cardiol*. 2018;264:91–92. doi:10.1016/j.ijcard.2018.03.113.
9. Issa M, Alqahtani F, Berzingi C, et al. Impact of acute diabetes decompensation on outcomes of diabetic patients admitted with ST-elevation myocardial infarction. *Diabetol Metab Syndr*. 2018;10(1):57. doi:10.1186/s13098-018-0357-y.
10. Faruqi TA, Hanhan UA, Orlowski JP, Laun KS, Williams AL, Fiallos MR. Supraventricular tachycardia with underlying atrial flutter in a diabetic ketoacidosis patient. *Clin Diabetes*. 2015;33(3):146–149. doi:10.2337/diaclin.33.3.146.
11. Cubbon RM, Kearney MT. Review: Acute metabolic derangement and the heart. *Diabetes Vasc Dis*. 2007;7(5):218. doi:10.1177/14746514070070050401.
12. Klevay LM, Milne DB. Low dietary magnesium increases supraventricular ectopy. *Am J Clin Nutr*. 2002;75(3):550–554. doi:10.1093/ajcn/75.3.550.
13. Orchard CH, Cingolani HE. Acidosis and arrhythmias in cardiac muscle. *Cardiovasc Res*. 1994;28(9):1312–1319. doi:10.1093/cvr/28.9.1312.
14. Youssef OI, Farid SM. QTc and QTd in children with type 1 diabetes mellitus during diabetic ketoacidosis. *ISRN Pediatr*. 2012;2012:1–4. doi:10.5402/2012/619107.
15. Lynge TH, Svane J, Pedersen-Bjergaard U, et al. Sudden cardiac death among persons with diabetes aged 1-49 years: a 10-year nationwide study of 14 294 deaths in Denmark. *Eur Heart J*. 2020;41(28):2699–2706. doi:10.1093/eurheartj/ehz891.
16. Sehgal V, Ulmer B. Clinical conundrums in the management of diabetic ketoacidosis in the elderly. *J Transl Int Med*. 2019;7(1):10–14. doi:10.2478/jtim-2019-0003.

Avocations

TO MY DAUGHTERS

When you took your first step my heart trembled inside
But I kept my cool.

Your first lesson to ride a bicycle was taxing
My hands clung to your seat to keep you steady
I kept running till you went around the corner
And you left me with the memories

Now these hands are weaker but still willing to prop you
Till the last ounce of strength
Your each wound hurt me; each bruise stung
I did not shake the feeling off or I did not wish to

I was a willing partner in carrying you on my shoulder
And pace the floor at night to quell your earache
I did not like the slimy feeling, but do you know?
I did not mind the slobber of your cutting teeth

Your first walk to school, I still remember
Every tiny step you took was an elephant on my chest
I kept staring at you as if I was in the fog
Till you were lost in the excitement of school

I shared your heart breaks, but never let you know
Those days are long gone
Now the responsibility lies with your husband
But I still get the twinge!

 Dr. Khan (e-mail: AKhan@cancercenterassociates.com) is president of the Rena Tarbet Cancer Center, an oncologist on the medical staff of Baylor Medical Center at McKinney, and member and past president of the Poetry Society of Texas.